

04/08/97

13041777 BIOSIS Number: 99041777

Exclusive development of T cell neoplasms in mice transplanted with bone marrow expressing activated Notch alleles

Pear W S; Aster J C; Scott M L; Hasserjian R P; Soffer B; Sklar J; Baltimore D

Massachusetts Inst. Technol., Room 68-380, 77 Massachusetts Ave., Cambridge, MA 02139-4307, USA

Journal of Experimental Medicine 183 (5). 1996. 2283-2291.

Full Journal Title: Journal of Experimental Medicine

ISSN: 0022-1007

Language: ENGLISH

Print Number: Biological Abstracts Vol. 102 Iss. 002 Ref. 023950

Notch is a highly conserved transmembrane protein that is involved in cell fate decisions and is found in organisms ranging from *Drosophila* to humans. A human homologue of Notch, TAN1, was initially identified at the chromosomal breakpoint of a subset of T-cell lymphoblastic leukemias/lymphomas containing a t(7;9) chromosomal translocation; however, its role in oncogenesis has been unclear. Using a bone marrow reconstitution assay with cells containing retrovirally transduced TAN1 alleles, we analyzed the oncogenic potential of both nuclear and extranuclear forms of truncated TAN1 in hematopoietic cells. Although the Moloney leukemia virus long terminal repeat drives expression in most hematopoietic cell types, retroviruses encoding either form of the TAN1 protein induced clonal leukemias of exclusively immature T cell phenotypes in apprx 50% of transplanted animals. All tumors overexpressed truncated TAN1 of the size and subcellular localization predicted from the structure of the gene. These results show that TAN1 is an oncoprotein and suggest that truncation and overexpression are important determinants of transforming activity. Moreover, the murine tumors caused by TAN1 in the bone marrow transplant model are very similar to the TAN1-associated human tumors and suggest that TAN1 may be specifically oncotropic for T cells.

14/7/9 (Item 9 from file: 5)

DIALOG(R) File 5:BIOSIS PREVIEWS(R)

(c) 1997 BIOSIS. All rts. reserv.

12098006 BIOSIS Number: 98698006

Epithelial expression and chromosomal location of human TLE genes:

Implications for notch signaling and neoplasia

Liu Y; Dehni G; Purcell K J; Sokolow J; Carcangiu M L; Artavanis-Tsakonas S; Stifani S

Montreal Neurol. Inst., 3801 University St., Montreal, PQ H3A 2B4, Canada Genomics 31 (1). 1996. 58-64.

Full Journal Title: Genomics

ISSN: 0888-7543

Language: ENGLISH

Print Number: Biological Abstracts Vol. 101 Iss. 007 Ref. 098287

The TLE genes are the human homologues of *Drosophila* groucho, a member of the Notch signaling pathway. This pathway controls a number of different gene family during epithelial determination and carcinogenesis. We show that expression of individual TLE genes correlates with immature epithelial cells that are progressing toward their terminally differentiated state, suggesting a role during epithelial differentiation. In both normal tissues and conditions resulting from incorrect or incomplete maturation events, such as metaplastic and neoplastic transformations, TLE expression is elevated and coincides with Notch expression, implicating these molecules

in the maintenance of the undifferentiated state in epithelial cells. We also show that TLE1 and TLE2 are organized in a tandem array at chromosomal location 19p13.3, while TLE3 maps to 15q22.

14/7/10 (Item 10 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
(c) 1997 BIOSIS. All rts. reserv.

11778798 BIOSIS Number: 98378798
Alterations in Notch signaling in neoplastic lesions of the human cervix
Zagouras P; Stifani S; Blaumueller C M; Carcangiu M L; Artavanis-Tsakonas
S

Dep. Biol., Yale Univ., New Haven, CT 06536, USA
Proceedings of the National Academy of Sciences of the United States of
America 92 (14). 1995. 6414-6418.

Full Journal Title: Proceedings of the National Academy of Sciences of
the United States of America

ISSN: 0027-8424

Language: ENGLISH

Print Number: Biological Abstracts Vol. 100 Iss. 005 Ref. 070636

The development of cancer is a cellular process that reflects and is partly driven by alterations in cell determination. Mutations in various molecules responsible for cell determination have been identified as being oncogenic, but little is known about the involvement of normal cell fate-determining mechanisms in the oncogenic process. The Notch pathway defines an evolutionarily conserved, general cell interaction mechanism that controls fundamental aspects of cell determination during vertebrate and invertebrate development. We have explored the involvement of the human Notch pathway in human cervical tissues, which define a cellular environment where cell fate changes take place and where neoplastic conditions have been well characterized. Our evidence suggests that Notch expression is associated with cell populations that are undergoing cell fate changes and that Notch activity can be used to monitor cell fate abnormalities in cervical as well as other epithelial neoplasias.

14/7/11 (Item 11 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
(c) 1997 BIOSIS. All rts. reserv.

11572298 BIOSIS Number: 98172298

Drosophila in cancer research: The first fifty tumor suppressor genes
Watson K L; Justice R W; Bryant P J

Dep. Molecular Cellular Biol., Harvard Univ., Cambridge, MA 02138, USA
Journal of Cell Science 0 (SUPPL. 18). 1994. 19-33.

Full Journal Title: Journal of Cell Science

ISSN: 0021-9533

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 008 Ref. 112601

Print Number: Biological Abstracts/RRM Vol. 047 Iss. 005 Ref. 069789

In Drosophila, over 50 genes have been identified in which loss-of-function mutations lead to excess cell proliferation in the embryo, in the central nervous system, imaginal discs or hematopoietic organs of the larva, or in the adult gonads. Twenty-two of these genes have been cloned and characterized at the molecular level, and nine of them show clear homology to mammalian genes. Most of these mammalian genes had not been previously implicated in cell proliferation control. Overgrowth in

some of the mutants involves conversion to a cell type that, in normal development, shows more cell proliferation than the original cell type. Thus the neurogenic mutants, including Notch, show conversion of epidermal cells to neuroblasts, leading to the 'neurogenic' phenotype of excess nervous tissue. The ovarian tumor mutants show conversion of the female germ line to a cell type resembling the male germ line, which undergoes more proliferation than the female germ line. Mutations of the fat locus cause hyperplastic overgrowth of imaginal discs, in which the epithelial structure is largely intact. The predicted fat protein product is a giant relative of cadherins, supporting indications from human cancer that cadherins play an important role in tumor suppression. Mutations in the lethal(2)giant larvae and lethal(1)discs large genes cause neoplastic overgrowth of imaginal discs as well as the larval brain. The dig gene encodes a membrane-associated guanylate kinase homolog that is localized at septate junctions between epithelial cells. This protein is a member of a family of homologs that also includes two proteins found at mammalian tight junctions (ZO-1 and ZO-2) and a protein found at mammalian synaptic junctions (PSD-95/SAP90). Genes in which mutations cause blood cell overproduction include aberrant immune response-8, which encodes the Rps6 ribosomal protein and hopscotch, which encodes a putative non-receptor protein tyrosine kinase. The gene products identified by ovarian tumor mutants do not show clear amino acid sequence homology to known proteins. Drosophila provides an opportunity to rapidly identify and characterize tumor suppressor genes, many of which have mammalian homologs that might also be involved in cell proliferation control and tumor suppression.

14/7/12 (Item 12 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
(c) 1997 BIOSIS. All rts. reserv.

11494818 BIOSIS Number: 98094818

Localization of blood vessels and qualitative assessment of blood flow in ovarian tumors

Maly Z; Riss P; Deutinger J

Heinrichova 18, CZ-60200 Brno, Czech Republic

Obstetrics & Gynecology 85 (1). 1995. 33-36.

Full Journal Title: Obstetrics & Gynecology

ISSN: 0029-7844

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 005 Ref. 065228

Objective: To study the localization of blood vessels within a tumor and the shape of the flow curve as a method of assessing ovarian neoplasms.

Methods: We studied 39 patients with malignant tumors and 63 patients with benign ovarian tumors by means of vaginal color Doppler ultrasound, noting the localization of blood vessels in the tumors, the shape of the flow curve, and peripheral resistance. Results: Blood vessels could be visualized in 95% of the malignant tumors and in 70% of the benign tumors. Blood vessels tended to be localized centrally (65 versus 5%) in malignant tumors and peripherally in benign tumors (65 versus 0%). A diastolic notch was seen in 89% of the benign tumors, but in none of the malignant tumors. The mean resistance index (RI) +- standard deviation was 0.48 +- 0.19 in malignant and 0.69 +- 0.09 in benign tumors (P < .05). The corresponding values for the pulsatility index (PI) were 0.56 +- 0.13 and 1.06 +- 0.07, respectively (P < .01). Conclusions: Low RI and PI values are general indicators of tumor growth. The localization of blood vessels within an ovarian tumor and the presence or absence of a diastolic notch are the most useful variables in the evaluation of ovarian tumors.

14/7/18 (Item 18 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
(c) 1997 BIOSIS. All rts. reserv.

10110234 BIOSIS Number: 95110234

DLK A PUTATIVE MAMMALIAN HOMEOTIC GENE DIFFERENTIALLY EXPRESSED IN SMALL CELL LUNG CARCINOMA AND NEUROENDOCRINE TUMOR CELL LINE

LABORDA J; SAUSVILLE E A; HOFFMAN T; NOTARIO V
CENTER BIOL. RESEARCH, FDA., 8800 ROCKVILLE PIKE, BLDG. 29, BETHESDA, MD 20892, USA.

J BIOL CHEM 268 (6). 1993. 3817-3820. CODEN: JBCHA

Full Journal Title: Journal of Biological Chemistry

Language: ENGLISH

Gastrin releasing peptide is mitogenic for mouse Swiss 3T3 fibroblasts and certain human small cell lung carcinoma (SCLC) cells but not for mouse Balb/c 3T3 fibroblasts. To identify new molecules associated with the gastrin releasing peptide-responsive phenotype, clones isolated from a differential cDNA library between Swiss and Balb/c 3T3 fibroblasts were used to screen for their expression in human SCLC cell lines. Using this approach, we have isolated and characterized human and mouse cDNA clones encoding a novel protein. This protein is a putative transmembrane protein belonging to the epidermal growth factor-like superfamily. In vitro transcription and translation studies detect a 42-kDa protein, in agreement with the size predicted from the translated cDNA sequence. This protein (termed Delta-like or dlk) is highly homologous to invertebrate homeotic proteins, including Delta, and Notch, the products of neurogenic loci involved in normal neural differentiation in *Drosophila*. dlk is expressed in tumors with neuroendocrine features, such as neuroblastoma, pheochromocytoma, and a subset of SCLC cells lines. However, its expression in normal tissues is restricted to the adrenal gland and placenta. These data suggest that dlk may be involved in neuroendocrine differentiation and, because of its cellular location and restricted expression in normal tissues, it may be a potential therapeutic target in neuroendocrine tumors, particularly SCLC.

14/7/21 (Item 21 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
(c) 1997 BIOSIS. All rts. reserv.

8646875 BIOSIS Number: 92111875

TAN-1 THE HUMAN HOMOLOG OF THE DROSOPHILA NOTCH GENE IS BROKEN BY CHROMOSOMAL TRANSLOCATIONS IN T LYMPHOBLASTIC NEOPLASMS

ELLISEN L W; BIRD J; WEST D C; SORENG A L; REYNOLDS T C; SMITH S D; SKLAR J

STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305.

CELL 66 (4). 1991. 649-662. CODEN: CELLB

Full Journal Title: Cell

Language: ENGLISH

Previously we described joining of DNA in the beta. T cell receptor gene to DNA of an uncharacterized locus in a t(7;9)(q34;q34.3) chromosomal translocation from a case of human lymphoblastic leukemia (T-ALL). We now show that the locus on chromosome 9 contains a gene highly homologous to the *Drosophila* gene Notch. Transcripts of the human gene, for which we propose the name TAN-1, and its murine counterpart are present in many normal human fetal and adult mouse tissues, but are most abundant in

lymphoid tissues. In t(7;9) (q34;q34.3) translocations from three cases of T-ALL, the breakpoints occur within 100 bp of an intron in TAN-1, resulting in truncation of TAN-1 transcripts. These observations suggest that TAN-1 may be important for normal lymphocyte function and that alteration of TAN-1 may play a role in the pathogenesis of some T cell neoplasms.

14/7/44 (Item 7 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 1997 Elsevier Science B.V. All rts. reserv.

9978677 EMBASE No: 96166337

T cell leukemia-associated human Notch/translocation-associated Notch homologue has IkappaB-like activity and physically interacts with nuclear factor-kappaB proteins in T cells

Guan E.; Wang J.; Laborda J.; Norcross M.; Baeuerle P.A.; Hoffman T. Division of Monoclonal Antibodies, Federal Drug Administration, Ctr. for Biologics Evaluation/Res., 8800 Rockville Pike, Bethesda, MD 20892 USA Journal of Experimental Medicine (USA) , 1996, 183/5 (2025-2032) CODEN: JEMEA ISSN: 0022-1007

LANGUAGES: English SUMMARY LANGUAGES: English

Translocation-associated Notch homologue (TAN-1), a gene originally cloned from the translocation breakpoint of a human T cell leukemia carrying a 9:7(q34.3) translocation, encodes a protein belonging to the Notch/Lin- 12/Glp-1 receptor family. These receptors mediate the specification of numerous cell fates during development in invertebrates and vertebrates. The intracellular portion of Notch/TAN-1 contains six ankyrin repeats that are similar to those found in cytoplasmic IkappaB proteins. IkappaB proteins are specific inhibitors of nuclear factor (NF)-kappaB/Rel transcription factors. Here we show that TAN-1 has functional properties of an IkappaB-like regulator with specificity for the NF-kappaB p50 subunit. A recombinant polypeptide corresponding to the cytoplasmic portion of TAN-1 (TAN-1(C)) specifically inhibited the DNA binding of p50-containing NF-kappaB complexes. When overexpressed in an appropriate cell line, TAN-1(C) prevented kappaB-dependent transactivation in transient reporter gene assays in a fashion similar to the structurally related protein, Bcl-3. TAN-1(C) could activate kappaB-dependent gene expression by attenuating the inhibitory effect of an excess of p50 homodimers. Immunoprecipitation experiments showed that the TAN-1 from a T cell line is associated with NF-kappaB containing p50 and p65 subunits. These observations indicate that TAN-1(C) may directly engage NF-kappaB transcription factors and modulate nuclear gene expression.

14/7/51 (Item 14 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 1997 Elsevier Science B.V. All rts. reserv.

9638945 EMBASE No: 95197896

Functional analysis of the TAN-1 gene, a human homolog of Drosophila notch

Aster J.; Pear W.; Hasserjian R.; Erba H.; Davi F.; Luo B.; Scott M.; Baltimore D.; Sklar J.

Department of Pathology, Harvard Medical School, Brigham and Women's Hospital, Boston, MA 02115 USA

Cold Spring Harbor Symposia on Quantitative Biology (USA) , 1994, 59/- (125-136) CODEN: CSHSA ISSN: 0091-7451

LANGUAGES: English

?

PLEASE ENTER A COMMAND OR BE LOGGED OFF IN 5 MINUTES

?t s14/7/108,113,122,148,162,163,164,165,
166,167,168,171,172,173,174,176,177,178,180

>>>Format 7 is not valid in file 143

14/7/108 (Item 6 from file: 144)

DIALOG(R)File 144:Pascal

(c) 1997 INIST/CNRS. All rts. reserv.

12471360 PASCAL No.: 96-0134151

Epithelial expression and chromosomal location of human TLE genes :
implications for notch signaling and neoplasia

YANLING LIU; GHASSAN DEHNI; PURCELL K J; SOKOLOW J; CARCANGIU M L;
ARTAVANIS-TSAKONAS S; STIFANI S

McGill univ., Montreal neurological inst., Montreal PQ H3A 2B4, Canada

Journal: Genomics : (San Diego, CA), 1996, 31 (1) 58-64

ISSN: 0888-7543 Availability: INIST-21389; 354000052959520080

No. of Refs.: 26 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: USA

Language: English

The TLE genes are the human homologues of *Drosophila* groucho, a member of the Notch signaling pathway. This pathway controls a number of different cell-fate choices in invertebrates and vertebrates. We are interested in investigating the functions of the TLE gene family during epithelial determination and carcinogenesis. We show that expression of individual TLE genes correlates with immature epithelial cells that are progressing toward their terminally differentiated state, suggesting a role during epithelial differentiation. In both normal tissues and conditions resulting from incorrect or incomplete maturation events, such as metaplastic and neoplastic transformations, TLE expression is elevated and coincides with Notch expression, implicating these molecules in the maintenance of the undifferentiated state in epithelial cells. We also show that TLE1 and TLE2 are organized in a tandem array at chromosomal location 19p13.3, while TLE3 maps to 15q22.

14/7/113 (Item 4 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

(c) format only 1997 Knight-Ridder Info. All rts. reserv.

08748890 95232495

Notch signaling.

Artavanis-Tsakonas S; Matsuno K; Fortini ME

Howard Hughes Medical Institute, Boyer Center for Molecular Medicine,
Yale University, New Haven, CT 06536, USA.

Science (UNITED STATES) Apr 14 1995, 268 (5208) p225-32, ISSN
0036-8075 Journal Code: UJ7

Contract/Grant No.: NS26084, NS, NINDS

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

The Notch/Lin-12/Glp-1 receptor family mediates the specification of numerous cell fates during development in *Drosophila* and *Caenorhabditis elegans*. Studies on the expression, mutant phenotypes, and developmental consequences of unregulated receptor activation have implicated these proteins in a general mechanism of local cell signaling, which includes

interactions between equivalent cells and between different cell types. Genetic approaches in flies and worms have identified putative components of the signaling cascade, including a conserved family of extracellular ligands and two cellular factors that may associate with the Notch Intracellular domain. One factor, the *Drosophila* Suppressor of Hairless protein, is a DNA-binding protein, which suggests that Notch signaling may involve relatively direct signal transmission from the cell surface to the nucleus. Several vertebrate Notch receptors have also been discovered recently and play important roles in normal development and tumorigenesis. (65 Refs.)

14/7/122 (Item 13 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 1997 Knight-Ridder Info. All rts. reserv.

07125808 92260975

Cancer, chromosomes, and genes.

Nowell PC

Department of Pathology and Laboratory Medicine, University of Pennsylvania, School of Medicine, Philadelphia.

Lab Invest (UNITED STATES) Apr 1992, 66 (4) p407-17, ISSN 0023-6837

Journal Code: KZ4

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

(67 Refs.)

14/7/148 (Item 1 from file: 156)

DIALOG(R) File 156: Toxline(R)

(c) format only 1997 Knight-Ridder Info. All rts. reserv.

01819547 Subfile: CRISP-95-CB08756-07

THE TRANSGENIC MOUSE AS A MODEL SYSTEM TO STUDY GENE FUNCTION AND REGULATION

MERLINO GT

NCI, NIH

Source: Crisp Data Base National Institutes Of Health

Language: ENGLISH

Document Type: Research

Spon. Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, DIVISION OF CANCER BIOLOGY AND DIAGNOSIS

Contract Number: 1Z01CB08756-07

Award Type: Intramural Project

RPROJ/CRISP Transgenic technology, in which foreign DNA is stably introduced into the mammalian gene line, represents a method to address basic biological questions that is both powerful and versatile. We are using this exciting technology to examine the role of growth factors, receptors and oncogenes in tumorigenesis, and to establish useful and novel animal models to aid in the study of pathogenesis in human disease. Transforming growth factor alpha (TGF alpha) stimulates cellular proliferation by binding to the epidermal growth factor (EGF) receptor and activating its tyrosine kinase. Perturbation of this signal transduction pathway can transform cells in culture, and has been implicated in human oncogenesis. To test this hypothesis *in vivo*, mice were made harboring a human TGFalpha transgene. Overexpression of TGFalpha was found to induce hepatocellular carcinoma, mammary adenocarcinoma, pancreatic metaplasia and fibrosis, and a hypertrophic gastropathy resembling Menetrier's disease.

Detailed molecular analysis of lesions in these mice has confirmed that TGFalpha promotes tumor formation and plays a role in tumor progression. Analysis of double transgenic mice demonstrated that TGFalpha and the c-myc nuclear protooncogene act in a synergistic fashion in hepatocarcinogenesis. Furthermore, TGFalpha was able to collaborate with diverse chemical agents in the development of liver tumors, including genotoxic initiators and nongenotoxic promoters. We have generated mice bearing transgenes encoding other relevant growth and differentiation factors. Transgenic mice made with an activated form of an EGF-related gene, int-3, which contains numerous EGF repeat- sequences and is a member of the Notch gene family, develop severe hyperplastic and developmental lesions of multiple secretory glands and cancer of the salivary and mammary glands. These findings demonstrate in vivo that expression of the activated int-3 gene causes deregulation of normal developmental controls and hyperproliferation of glandular epithelia. In another study, mice overexpressing a transforming growth factor beta1 (TGFbeta1) transgene in the pregnant mammary gland were unable to lactate due to the inhibition of the formation of lobuloalveolar structures and suppression of endogenous milk production. These results strongly suggest that TGFbeta1 plays an important role in regulating the development and function of the mammary gland.

14/7/162 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 1997 Derwent Publ Ltd. All rts. reserv.

priority to this appn

164909 DBA Accession No.: 94-07460 PATENT

Notch protein and antisense DNA - application in carcinoma diagnosis,
therapy and gene therapy

PATENT ASSIGNEE: Univ.Yale 1994

PATENT NUMBER: WO 9407474 PATENT DATE: 940414 WPI ACCESSION NO.:
94-135180 (9416)

PRIORITY APPLIC. NO.: US 83590 APPLIC. DATE: 930625

NATIONAL APPLIC. NO.: WO 93US9338 APPLIC. DATE: 930930

LANGUAGE: English

ABSTRACT: A pharmaceutical composition comprising a Notch protein (A) and a carrier is claimed. More specifically, the composition comprises a human Notch protein encoded by a specified DNA sequence which is bound by an antibody to a Notch protein. The following are also claimed: (1) a pure human Notch protein homolog of specified protein sequence; (2) nucleic acid encoding the protein of (1); (3) a recombinant cell containing the nucleic acid of (2); (4) a composition comprising a Notch protein or derivative (e.g. chimeric protein); (5) a composition comprising a molecule which antagonizes the function of a Notch protein; and (6) the use of the composition of (5) for treatment of cervix carcinoma, mamma carcinoma or colon carcinoma. In (4), the chimeric protein may include functionally active portions of the Notch protein encoded by human cDNA contained in plasmid pHN3k (ATCC 68609) and plasmid pHN5k (ATCC 68611). The therapeutic composition includes Notch proteins and analogs, antibodies, nucleic acid encoding the analogs, antisense nucleic acids, etc. which bind and interact with Notch proteins, their encoding nucleic acids or antibodies. (232pp)

14/7/163 (Item 1 from file: 358)

DIALOG(R)File 358:Current BioTech Abs
Royal Soc Chem & DECHEMA . All rts. reserv.

074382 CBA Acc. No.: 13-09-007173 DOC. TYPE: Patent
Therapeutic and diagnostic method and compositions based on Notch proteins
and nucleic acids.

AUTHOR: Artavanis-Tsakonas, S.; Fehon, R. G.; Zagouras, P.; Blaumeuller, C.
M.

CORPORATE SOURCE: Yale Univ., New Haven, CT 06520, USA

CODEN: PIXXD2

PATENT NUMBER: WO 9407474

PATENT APPLICATION: US 955012 (920930)

PUBLICATION DATE: 14 Apr 1994 (940414) LANGUAGE: English

ABSTRACT: Therapeutic and diagnostic methods and compositions based on Notch proteins and nucleic acids are disclosed, together with the sequences of human Notch DNA and the encoded Notch protein. Disorders of cell fate or differentiation are treated by administering the Notch proteins, antibodies thereto, nucleic acids encoding the Notch proteins, antisense Notch nucleic acids, and toporhythmic proteins and derivatives which bind to or interact with Notch proteins. The methods are especially useful in cancer therapy.

14/7/164 (Item 1 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

(c) 1997 American Chemical Society. All rts. reserv.

125319671 CA: 125(25)319671w DISSERTATION

Structural and expression analyses of human homologs of the drosophila Notch protein (*Drosophila melanogaster*, cell signaling)

AUTHOR(S): Blaumueller, Christine Marie

LOCATION: Yale Univ., New Haven, CT, USA

DATE: 1996 PAGES: 250 pp. CODEN: DABBBA LANGUAGE: English CITATION:
Diss. Abstr. Int., B 1996, 57(6), 3564 AVAIL: Univ. Microfilms Int., Order
No. DA9635411

SECTION:

CA203004 Biochemical Genetics

CA206XXX General Biochemistry

CA213XXX Mammalian Biochemistry

IDENTIFIERS: *Drosophila* gene Notch2 expression human cancer

DESCRIPTORS:

Lung, neoplasm...

human; structural and expression analyses of human homologs of the drosophila Notch protein (*Drosophila melanogaster*, cell signaling)

Gene, animal...

Notch2, human; structural and expression analyses of human homologs of the drosophila Notch protein (*Drosophila melanogaster*, cell signaling)

Drosophila melanogaster... Glycoproteins, specific or class, gene Notch...

Signal transduction, biological...

structural and expression analyses of human homologs of the drosophila Notch protein (*Drosophila melanogaster*, cell signaling)

14/7/165 (Item 2 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

(c) 1997 American Chemical Society. All rts. reserv.

125267553 CA: 125(21)267553n PATENT

Serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

INVENTOR(AUTHOR): Ish-Horowicz, David; Henrique, Domingos M. P.; Lewis,

Julian H.; Myat, Anna M.; Artavanis-Tsakonas, Spyridon; Mann, Robert S.; Gray, Grace E.

LOCATION: USA

ASSIGNEE: Yale University; Imperial Cancer Research Technology, Ltd.

PATENT: PCT International ; WO 9627610 A1 DATE: 960912

APPLICATION: WO 96US3172 (960307) *US 400159 (950307)

PAGES: 161 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/00A; A01N-037/18B; A01N-043/04B; C07H-017/00B; C12N-005/00B; C12P-021/06B

DESIGNATED COUNTRIES: AL; AM; AU; AZ; BB; BG; BR; BY; CA; CN; CZ; EE; FI; GE; HU; IS; JP; KG; KP; KR; KZ; LK; LR; LS; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; TJ; TM; TR; TT; UA; US; UZ; VN; AM; AZ; BY

DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

SECTION:

CA203003 Biochemical Genetics

CA212XXX Nonmammalian Biochemistry

CA213XXX Mammalian Biochemistry

IDENTIFIERS: Serrate gene human mouse chicken Xenopus

DESCRIPTORS:

Cell proliferation...

disorders of, treatment with agonists or antagonists of Serrate protein; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Plasmid and Episome,pBS39...

human Serrate-1 gene cDNA on; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Glycoproteins, specific or class, gene Notch...

inhibitors of, as neoplasm inhibitors; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Development,nonmammalian...

Notch gene expression in chicken as function of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Development,mammalian...

Notch gene expression in mouse as function of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Blood vessel... Embryo,limb bud... Embryo,primitive streak... Embryo,somite

... Eye,lens... Eye,retina... Hair,vibrissa, follicle... Heart... Kidney...

Nerve center and Ganglion,spinal... Nervous system,neural tube... Notochord

... Salivary gland... Thymus gland...

Notch gene expression in; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Protein sequences...

of Serrate gene products of human and chicken; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Deoxyribonucleic acid sequences,complementary...

of Serrate genes of human and chicken; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Plasmid and Episome...

pBS15, human Serrate-1 gene cDNA on; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Plasmid and Episome...

pBS3-2, human Serrate-1 gene cDNA on; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Embryo,mesoderm...

presomitic, Notch gene expression in; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses
Neoplasm inhibitors...

seminoma, Serrate protein derivs. inhibiting Notch protein as; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Gene, animal, Serrate... Proteins, specific or class, gene Serrate... serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Intestine, neoplasm, colon, inhibitors... Lung, neoplasm, inhibitors... Mammary gland, neoplasm, inhibitors... Neoplasm inhibitors... Neoplasm inhibitors, colon... Neoplasm inhibitors, lung... Neoplasm inhibitors, mammary gland... Neoplasm inhibitors, melanoma... Neoplasm inhibitors, uterus cervix... Uterus, neoplasm, cervix, inhibitors...

Serrate protein derivs. inhibiting Notch protein as; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Gene, animal...

Serrate-1, cloning of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Gene, animal...

Serrate-2, cloning of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Deoxyribonucleic acids, complementary, antisense...

to Serrate gene, therapeutic uses of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Antibodies... Antibodies, monoclonal...

to Serrate proteins; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Testis, neoplasm, seminoma...

treatment of, Serrate protein derivs. inhibiting Notch protein for; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

Nervous system, central, disease...

treatment of; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

CAS REGISTRY NUMBERS:

182328-94-5 182372-88-9 182372-90-3 182372-91-4 amino acid sequence; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

182328-93-4 182372-87-8 182372-89-0 nucleotide sequence; serrate genes and proteins of human and other vertebrates and their applications and therapeutic uses

14/7/166 (Item 3 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

(c) 1997 American Chemical Society. All rts. reserv.

123276008 CA: 123(21)276008z PATENT

Drosophila melanogaster and human gene deltex proteins, nucleic acids, and antibodies, and related methods and compositions

INVENTOR(AUTHOR): Artavanis-Tsakonas, Spyridon; Busseau, Isabelle; Diederich, Robert J.; Xu, Tian; Matsuno, Kenji

LOCATION: USA

ASSIGNEE: Yale University

PATENT: PCT International ; WO 9519779 A1 DATE: 950727

APPLICATION: WO 95US825 (950120) *US 185432 (940121)

PAGES: 151 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-035/12A;
C07H-017/00B; C07K-001/00B; C07K-014/00B; C07K-016/00B; C12N-001/00B;
C12N-005/00B; C12N-015/00B; C12Q-001/00B; C12Q-001/68B; G01N-033/53B

DESIGNATED COUNTRIES: AM; AU; BB; BG; BR; BY; CA; CN; CZ; EE; FI; GE; HU;
JP; KE; KG; KR; KZ; LK; LR; LT; LV; MD; MG; MN; MW; MX; NO; NZ; PL; RO; RU;
SD; SI; SK; TJ; TT; UA; UZ; VN DESIGNATED REGIONAL: KE; MW; SD; SZ; AT; BE;
CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG;
CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

SECTION:

CA201006 Pharmacology

CA203XXX Biochemical Genetics

CA206XXX General Biochemistry

CA212XXX Nonmammalian Biochemistry

CA213XXX Mammalian Biochemistry

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: gene deltex protein *Drosophila* human cancer, tumor inhibitor
gene deltex protein sequence

DESCRIPTORS:

Ankyrins... Antibodies... Cytoplasm... Development, nonmammalian...

Gene, animal, deltex... Glycoproteins, specific or class, gene Notch...

Intestine, neoplasm, colon... Lung, neoplasm... Mammary gland, neoplasm...

Melanoma... Neoplasm inhibitors... Neoplasm... Nervous system, disease...

Testis, neoplasm, seminoma... Uterus, neoplasm, cervix...

Drosophila melanogaster and human gene deltex proteins, nucleic acids,
and antibodies, and related methods and compns.

Proteins, specific or class...

gene deltex; *Drosophila melanogaster* and human gene deltex proteins,
nucleic acids, and antibodies, and related methods and compns.

Protein sequences...

of *Drosophila melanogaster* gene deltex protein; *Drosophila melanogaster*
and human gene deltex proteins, nucleic acids, and antibodies, and
related methods and compns.

Deoxyribonucleic acid sequences...

of *Drosophila melanogaster* gene deltex; *Drosophila melanogaster* and
human gene deltex proteins, nucleic acids, and antibodies, and related
methods and compns.

Plasmid and Episome...

pCaSpeR; *Drosophila melanogaster* and human gene deltex proteins,
nucleic acids, and antibodies, and related methods and compns.

CAS REGISTRY NUMBERS:

169240-98-6P amino acid sequence of; *Drosophila melanogaster* and human
gene deltex proteins, nucleic acids, and antibodies, and related
methods and compns.

169240-97-5 nucleotide sequence of; *Drosophila melanogaster* and human gene
deltex proteins, nucleic acids, and antibodies, and related methods and
compns.

14/7/167 (Item 4 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

(c) 1997 American Chemical Society. All rts. reserv.

120130975 CA: 120(11)130975d DISSERTATION

TAN-1, the human homolog of *Drosophila* "Notch", is involved in
chromosomal translocations in human lymphoblastic neoplasia

AUTHOR(S): Ellisen, Leif William

LOCATION: Stanford Univ., Stanford, CA, USA

DATE: 1992 PAGES: 80 pp. CODEN: DABBBA LANGUAGE: English CITATION:

Diss. Abstr. Int. B 1993, 53(7), 3307 AVAIL: Univ. Microfilms Int., Order No. DA9234046

SECTION:

CA214001 Mammalian Pathological Biochemistry

CA203XXX Biochemical Genetics

IDENTIFIERS: gene TAN1 chromosome translocation lymphoblastic leukemia

DESCRIPTORS:

Leukemia, T-cell acute lymphocytic...

 gene TAN-1 translocation in, in human

Recombination, genetic, translocation...

 of gene TAN-1, in human T-cell acute lymphoblastic leukemia

Gene, animal...

 TAN-1, chromosomal translocation of, in human T-cell lymphoblastic leukemia

Chromosome, human 7...

 TAN-1 gene translocation from, in human T-cell lymphoblastic leukemia

14/7/168 (Item 1 from file: 434)

DIALOG(R) File 434: Scisearch(R) Cited Ref Sci

(c) 1997 Inst for Sci Info. All rts. reserv.

15505893 Genuine Article#: WL964 Number of References: 49

Title: Germ-line tumor formation caused by activation of glp-1, a *Caenorhabditis elegans* member of the Notch family of receptors

Author(s): Berry LW; Westlund B; Schedl T (REPRINT)

Corporate Source: WASHINGTON UNIV, SCH MED, DEPT GENET, CAMPUS BOX 8232, 4566 SCOTT AVE/ST LOUIS//MO/63110 (REPRINT); WASHINGTON UNIV, SCH MED, DEPT GENET/ST LOUIS//MO/63110

Journal: DEVELOPMENT, 1997, V124, N4 (FEB), P925-936

ISSN: 0950-1991 Publication date: 19970200

Publisher: COMPANY OF BIOLOGISTS LTD, BIDDER BUILDING CAMBRIDGE COMMERCIAL PARK COWLEY RD, CAMBRIDGE, CAMBS, ENGLAND CB4 4DL

Language: English Document Type: ARTICLE

Abstract: *Caenorhabditis elegans* germ-line proliferation is controlled by an inductive interaction between the somatic distal tip cell and the germ line, GLP-1, a member of the Notch family of transmembrane receptors, is required continuously in the germ line to transduce the proliferative signal, In the absence of GLP-1, all proliferative germ cells exit the mitotic cell cycle and enter meiotic prophase, We have characterized an activating mutation in glp-1, oz112gf, that has the opposite phenotype, Homozygous glp-1(oz112gf) hermaphrodites and males have a completely tumorous germ line in which germ cells never leave the mitotic cycle, In glp-1(oz112gf) heterozygotes, germ-line polarity is established correctly, but as adults age, the distal proliferative population expands leading to a late-onset tumorous phenotype, The mutant receptor is constitutively active, promoting proliferation in the absence of ligand, The normal distal-proximal spatial restriction of GLP-1 expression is lost in tumorous and late-onset tumorous animals; ectopically proliferating germ cells contain membrane-associated GLP-1, The correlation between proliferation and expression, both in wild-type where glp-1 signalling is limited by localized ligand and in glp-1(oz112gf) where signalling is ligand-independent, suggests that glp-1 signalling positively regulates GLP-1 expression, In addition to germ-line defects, glp-1(oz112gf) causes inappropriate vulval cell fate specification, A missense mutation in a conserved extracellular residue, Ser642, adjacent to the transmembrane domain, is sufficient to confer the glp-1(oz112gf) mutant

phenotypes. Two mammalian Notch family members, TAN-I and int-3, are proto-oncogenes. Thus, activating mutations in both invertebrate and vertebrate Notch family members can lead to tumor formation.

14/7/171 (Item 4 from file: 434)
DIALOG(R) File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

14774327 Genuine Article#: UK921 Number of References: 82
Title: MMTV-INDUCED MUTATIONS IN MOUSE MAMMARY-TUMORS - THEIR POTENTIAL RELEVANCE TO HUMAN BREAST-CANCER
Author(s): CALLAHAN R
Corporate Source: NCI,ONCOGENET SECT,TUMOR IMMUNOL & BIOL LAB,BLDG 10,ROOM 5B50/BETHESDA//MD/20892
Journal: BREAST CANCER RESEARCH AND TREATMENT, 1996, V39, N1, P33-44
ISSN: 0167-6806
Language: ENGLISH Document Type: ARTICLE
Abstract: In mouse mammary tumor virus (MMTV) infected mice, three identifiable stages of mammary tumorigenesis can be biologically defined: preneoplastic hyperplastic nodules, malignant tumor, and distant metastatic lesions (primarily in the lung). MMTV is a biological carcinogen which induces somatic mutations as consequence of its integration into the host cellular genome. Each stage of mammary tumorigenesis appears to result from the clonal outgrowth of cells containing additional integrated proviral MMTV genomes. This phenomenon has provided the basis for an approach to identify genes which, when affected, may contribute to progression through the different stages of mammary tumorigenesis. Eight different genes (Wnt1, Wnt3, Wnt10b, Fgf3, Fgf4, Fgf8, lnt3, and lnt6) have been shown to be genetically altered in multiple mammary tumors as a consequence of MMTV integration. Although the significance of the human homologs of these genes as targets for somatic mutation during human breast carcinogenesis is only now being explored, it is clear that this work has led to a new appreciation of the complexity of the genetic circuitry that is involved in the control of normal mammary gland growth and development. It seems likely that some of the mutations induced by MMTV, and the signaling pathways in which these target genes take part, will be relevant to the progression from preneoplastic lesions to distant metastasis in human breast cancer.

14/7/172 (Item 5 from file: 434)
DIALOG(R) File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

14627602 Genuine Article#: UB729 Number of References: 62
Title: SHOTGUN ENCODES DROSOPHILA E-CADHERIN AND IS PREFERENTIALLY REQUIRED DURING CELL REARRANGEMENT IN THE NEURECTODERM AND OTHER MORPHOGENETICALLY ACTIVE EPITHELIA
Author(s): TEPASS U; GRUSZYNKIDEFEO E; HAAG TA; OMATYAR L; TOROK T; HARTENSTEIN V
Corporate Source: UNIV TORONTO,DEPT ZOOL/TORONTO/ON MS5 1A1/CANADA/; UNIV CALIF LOS ANGELES,DEPT MOLEC CELLULAR DEV BIOL/LOS ANGELES//CA/90024; HUNGARIAN ACAD SCI,BIOL RES CTR,INST GENET/H-6701 SZEGED//HUNGARY/
Journal: GENES & DEVELOPMENT, 1996, V10, N6 (MAR 15), P672-685
ISSN: 0890-9369
Language: ENGLISH Document Type: ARTICLE

Abstract: Adhesion molecules of the cadherin superfamily have an important role during vertebrate development. The DE-cadherin homolog DE-cadherin is the first classic cadherin isolated from invertebrates. We report here that DE-cadherin is encoded by the shotgun (shg) gene. shg is expressed in most embryonic epithelia and decreases in cells that undergo epithelial-mesenchymal transitions like the mesoderm or neural precursors. Removal of both maternal and zygotic shg function leads to severe defects in all epithelia expressing shg, suggesting that DE-cadherin, similar to vertebrate classic cadherins, has a crucial role for the formation and/or maintenance of epithelial tissues. Interestingly, the analysis of different shg alleles indicates that the requirement for shg in a given epithelium depends on the degree of its morphogenetic activity. Only epithelia involved in extensive morphogenetic movements require zygotic shg function in addition to maternal expression. In support of this view we find that suppression of morphogenetic movements rescues the zygotic shg phenotype. We find that in zygotic shg nulls the level of D alpha-catenin and Armadillo at adherens junctions is dramatically reduced, surprisingly also in epithelia that differentiate normally and possess a zonula adherens.

14/7/173 (Item 6 from file: 434)
DIALOG(R) File 434: Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

13733132 Genuine Article#: QK899 Number of References: 158
Title: DROSOPHILA IN CANCER-RESEARCH - THE FIRST 50 TUMOR-SUPPRESSOR GENES
Author(s): WATSON KL; JUSTICE RW; BRYANT PJ
Corporate Source: HARVARD UNIV, DEPT MOLEC & CELLULAR
BIOL/CAMBRIDGE//MA/02138; UNIV CALIF IRVINE, CTR DEV
BIOL/IRVINE//CA/92717

Journal: JOURNAL OF CELL SCIENCE, 1994, S18, P19-33
ISSN: 0021-9533

Language: ENGLISH Document Type: REVIEW

Abstract: In *Drosophila*, over 50 genes have been identified in which loss-of-function mutations lead to excess cell proliferation in the embryo, in the central nervous system, imaginal discs or hematopoietic organs of the larva, or in the adult gonads. Twenty-two of these genes have been cloned and characterized at the molecular level, and nine of them show clear homology to mammalian genes. Most of these mammalian genes had not been previously implicated in cell proliferation control. Overgrowth in some of the mutants involves conversion to a cell type that, in normal development, shows more cell proliferation than the original cell type. Thus the neurogenic mutants, including Notch, show conversion of epidermal cells to neuroblasts, leading to the 'neurogenic' phenotype of excess nervous tissue. The ovarian tumor mutants show conversion of the female germ line to a cell type resembling the male germ line, which undergoes more proliferation than the female germ line. Mutations of the fat locus cause hyperplastic overgrowth of imaginal discs, in which the epithelial structure is largely intact. The predicted fat protein product is a giant relative of cadherins, supporting indications from human cancer that cadherins play an important role in tumor suppression. Mutations in the lethal(2)giant larvae and lethal(1)discs large genes cause neoplastic over-growth of imaginal discs as well as the larval brain. The dig gene encodes a membrane-associated guanylate kinase homolog that is localized at septate junctions between epithelial cells. This protein is a member of a family of homologs that also includes two proteins

found at mammalian tight junctions (ZO-1 and ZO-2) and a protein found at mammalian synaptic junctions (PSD-95/SAP90). Genes in which mutations cause blood cell overproduction include aberrant immune response-8, which encodes the RpS6 ribosomal protein and hopscotch, which encodes a putative non-receptor protein tyrosine kinase. The gene products identified by ovarian tumor mutants do not show clear amino acid sequence homology to known proteins. *Drosophila* provides an opportunity to rapidly identify and characterize tumor suppressor genes, many of which have mammalian homologs that might also be involved in cell proliferation control and tumor suppression.

14/7/174 (Item 7 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

13560613 Genuine Article#: PX953 Number of References: 62
Title: AN OVEREXPRESSED GENE TRANSCRIPT IN SENESCENT AND QUIESCENT HUMAN FIBROBLASTS ENCODING A NOVEL PROTEIN IN THE EPIDERMAL GROWTH FACTOR-LIKE REPEAT FAMILY STIMULATES DNA-SYNTHESIS

Author(s): LECKACZERNIK B; LUMPKIN CK; GOLDSTEIN S

Corporate Source: JOHN L MCCLELLAN MEM VET ADM MED CTR, CTR GERIATR RES EDUC & CLIN, 4300 W 7TH ST, 151RES/LITTLE ROCK//AR/72205; UNIV ARKANSAS MED SCI HOSP, DEPT MED/LITTLE ROCK//AR/72205; UNIV ARKANSAS MED SCI HOSP, DEPT BIOCHEM & MOLECBIOL/LITTLE ROCK//AR/72205; UNIV ARKANSAS MED SCI HOSP, DEPT PEDIAT/LITTLE ROCK//AR/72205; ARKANSAS CHILDRENS HOSP, RES CTR/LITTLE ROCK//AR/72205

Journal: MOLECULAR AND CELLULAR BIOLOGY, 1995, V15, N1 (JAN), P120-128

ISSN: 0270-7306

Language: ENGLISH Document Type: ARTICLE

Abstract: We carried out subtractive enrichment of a cDNA library derived from mRNA of senescent human diploid fibroblasts (HDF) established from a subject with Werner syndrome of premature aging. By differential screening, we isolated an overexpressed cDNA sequence (S1-5) that codes for a novel protein containing epidermal growth factor (EGF)-like domains which match the EGF-like consensus sequences within several known extracellular proteins that play a role in cell growth, development, and cell signalling. S1-5 mRNA is overexpressed in Werner syndrome and senescent normal HDF, is induced by growth arrest of young normal cells, but is significantly decreased by high serum, conditions which promote cellular proliferation. Paradoxically, microinjection into young HDF of two different lengths of S1-5 mRNA, containing different putative AUG translational start sites, consistently stimulated rather than inhibited DNA synthesis by an apparent autocrine/paracrine mechanism. Thus, the S1-5 gene product may represent a negative and/or positive factor whose ultimate activity is modulated by the cell environment as occurs with other members of EGF-like family.

14/7/176 (Item 9 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

13545391 Genuine Article#: PX512 Number of References: 41
Title: THE HUMAN NOTCH1, NOTCH2, AND NOTCH3 GENES ARE LOCATED AT CHROMOSOME POSITIONS 9Q34, 1P13-P11, AND 19P13.2-P13.1 IN REGIONS OF NEOPLASIA-ASSOCIATED TRANSLOCATION

Author(s): LARSSON C; LARDELLI M; WHITE I; LENDAHL U
Corporate Source: KAROLINSKA INST, MED NOBEL INST, DEPT CELL & MOLEC
BIOL/S-17177 STOCKHOLM//SWEDEN/; KAROLINSKA INST, MED NOBEL INST, DEPT
CELL & MOLEC BIOL/S-17177 STOCKHOLM//SWEDEN/; KAROLINSKA HOSP, DEPT CLIN
GENET/S-17176 STOCKHOLM//SWEDEN/
Journal: GENOMICS, 1994, V24, N2 (NOV 15), P253-258
ISSN: 0888-7543
Language: ENGLISH Document Type: ARTICLE
Abstract: In *Drosophila* the Notch gene controls differentiation to various cell fates in many tissues. Three mammalian Notch homologs have recently been identified: Notch 1, 2, and 3. All three homologs are very highly conserved relative to the *Drosophila* Notch gene, which suggests that they are important for cell differentiation in mammals. This notion is supported by the previous finding of a truncated, translocated form of the human NOTCH1 gene (formerly TAN1) in three cases of leukemia. Given this genetic link between NOTCH1 and tumor formation, it is of interest to establish the chromosomal positions of the other two homologs. We report the identification of cosmid clones for the human NOTCH1, 2, and 3 genes. These clones were used as probes in fluorescence in situ hybridization to human metaphase chromosomes, and the results, combined with data from somatic cell hybrid panels, show that the NOTCH2 and 3 genes are located at positions 1p13-p11 and 19p13.2-p13.1, respectively, which are regions of neoplasia-associated translocation. (C) 1994 Academic Press, Inc.

14/7/177 (Item 10 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

13393826 Genuine Article#: PK060 Number of References: 48
Title: 3 GENES IN THE HUMAN MHC CLASS-III REGION NEAR THE JUNCTION WITH THE CLASS-II - GENE FOR RECEPTOR OF ADVANCED GLYCOSYLATION END-PRODUCTS, PBX2 HOMEobox GENE AND A NOTCH HOMOLOG, HUMAN COUNTERPART OF MOUSE MAMMARY-TUMOR GENE INT-3
Author(s): SUGAYA K; FUKAGAWA T; MATSUMOTO K; MITA K; TAKAHASHI E; ANDO A; INOKO H; IKEMURA T
Corporate Source: NATL INST GENET, DEPT EVOLUTIONARY GENET, YATA
1111/MISHIMA/SHIZUOKA 411/JAPAN/; NATL INST GENET, DEPT EVOLUTIONARY GENET/MISHIMA/SHIZUOKA 411/JAPAN/; GRAD UNIV ADV
STUDIES/MISHIMA/SHIZUOKA 411/JAPAN/; NATL INST RADIOL SCI/ANAGAWA/CHIBA
263/JAPAN/; TOKAI UNIV, SCH MED/ISEHARA/KANAGAWA 25911/JAPAN/
Journal: GENOMICS, 1994, V23, N2 (SEP 15), P408-419
ISSN: 0888-7543

Language: ENGLISH Document Type: ARTICLE
Abstract: Cosmid walking of about 250 kb from MHC class III gene CYP21 to class II was conducted. The gene for receptor of advanced glycosylation end products of proteins (RAGE, a member of immunoglobulin superfamily molecules), the PBX2 homeobox gene designated HOX12, and the human counterpart of the mouse mammary tumor gene int-3 were found. The contiguous RAGE and HOX12 genes were completely sequenced, and the human int-3 counterpart was partially sequenced and assigned to a Notch homolog. This human Notch homolog, designated NOTCH3, showed both the intracellular portion present in the mouse int-3 sequence and the extracellular portion absent in the int-3. It thus corresponds to the intact form of a Notch-type transmembrane protein. About 20 kb of dense Alu clustering was found just centromeric to the NOTCH3. (C) 1994 Academic Press, Inc.

14/7/178 (Item 11 from file: 434)
DIALOG(R) File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

12891144 Genuine Article#: BZ51X Number of References: 95
Title: FREQUENT MUTATIONS IN BREAST-CANCER
Author(s): CALLAHAN R; GALLAHAN D; SMITH G; CROPP C; MERLO G; DIELLA F;
LISCIA D; LIDEREAU R
Corporate Source: NCI,BLDG 10,ROOM 5B50/BETHESDA//MD/20892; SAN GIOVANNI
VECCHIO HOSP,USSL 1,PATHOL SECT/I-10123 TURIN//ITALY//; CTR RENE
HUGUENIN/ST CLOUD//FRANCE/
Journal: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, 1993, V698, P21-30
ISSN: 0077-8923
Language: ENGLISH Document Type: ARTICLE

14/7/180 (Item 13 from file: 434)
DIALOG(R) File 434:Scisearch(R) Cited Ref Sci
(c) 1997 Inst for Sci Info. All rts. reserv.

11736855 Genuine Article#: JG755 Number of References: 74
Title: EXPRESSION PATTERN OF MOTCH, A MOUSE HOMOLOG OF DROSOPHILA-NOTCH,
SUGGESTS AN IMPORTANT ROLE IN EARLY POSTIMPLANTATION MOUSE DEVELOPMENT
Author(s): DELAMO FF; SMITH DE; SWIATEK PJ; GENDRONMAGUIRE M; GREENSPAN RJ;
MCMAHON AP; GRIDLEY T
Corporate Source: ROCHE INST MOLEC BIOL, ROCHE RES CTR, DEPT CELL & DEV
BIOL/NUTLEY//NJ/07110; ROCHE INST MOLEC BIOL, ROCHE RES CTR, DEPT CELL
& DEV BIOL/NUTLEY//NJ/07110; ROCHE INST MOLEC BIOL, ROCHE RES CTR, DEPT
NEUROSCI/NUTLEY//NJ/07110
Journal: DEVELOPMENT, 1992, V115, N3 (JUL), P737&
Language: ENGLISH Document Type: ARTICLE
Abstract: The Notch gene of Drosophila encodes a large transmembrane protein involved in cell-cell interactions and cell fate decisions in the Drosophila embryo. To determine if a gene homologous to Drosophila Notch plays a role in early mouse development, we screened a mouse embryo cDNA library with probes from the *Xenopus* Notch homolog, *Xotch*. A partial cDNA clone encoding the mouse Notch homolog, which we have termed Motch, was used to analyze expression of the Motch gene. Motch transcripts were detected in a wide variety of adult tissues, which included derivatives of all three germ layers. Differentiation of P19 embryonal carcinoma cells into neuronal cell types resulted in increased expression of Motch RNA. In the postimplantation mouse embryo Motch transcripts were first detected in mesoderm at 7.5 days post coitum (dpc). By 8.5 dpc, transcript levels were highest in presomitic mesoderm, mesenchyme and endothelial cells, while much lower levels were detected in neuroepithelium. In contrast, at 9.5 dpc, neuroepithelium was a major site of Motch expression. Transcripts were also abundant in cell types derived from neural crest. These data suggest that the Motch gene plays multiple roles in patterning and differentiation of the early postimplantation mouse embryo.

?ds

Set	Items	Description
S1	83932	NOTCH
S2	45	MOTCH

S3 50 XOTCH
S4 12 TAN-1
S5 83970 S1 OR S2 OR S3 OR S4
S6 864597 MALIGNAN?
S7 1931474 NEOPLAS?
S8 1935814 CANCER
S9 1071457 CARCINOMA
S10 4014115 S6 OR S7 OR S8 OR S9
S11 444 S5 AND S10
S12 269 RD S11 (unique items)
S13 18935603 HUMAN
S14 184 S12 AND S13
S15 6401254 PATIENT O